

LESSON OF THE MONTH

Clinical, radiological, and therapeutic features of pleomorphic xanthoastrocytoma: report of three patients and review of the literature

Dirk Van Roost, Rudolf Kristof, Josef Zentner, Helmut K Wolf, Johannes Schramm

Department of
Neurosurgery
D Van Roost
R Kristof
J Zentner
J Schramm

Department of
Neuropathology,
University of Bonn,
Germany
H K Wolf

Correspondence to:
Dr Van Roost.

Received 13 April 1995
and in final revised form
29 January 1996
Accepted 9 February 1996

Abstract

Two out of three patients with pleomorphic xanthoastrocytoma were initially misdiagnosed and correctly interpreted only at tumour recurrence, with progression to malignancy in one. The third patient presented with a remarkably long history of epilepsy. Pleomorphic xanthoastrocytoma is a low grade astrocytoma that is still confused with other tumours. Because pleomorphic xanthoastrocytoma can become malignant even after many years of benign behaviour, a long term follow up is necessary.

(*J Neurol Neurosurg Psychiatry* 1996;60:690-692)

Keywords: pleomorphic xanthoastrocytoma; glioma; brain neoplasm

Pleomorphic xanthoastrocytoma, a low grade astrocytoma that mainly affects patients younger than 30, manifests itself by seizures in 75% of the patients and is still confused with other neoplasms. We report one patient who presented with a remarkably long history of epilepsy and two other patients who were initially misdiagnosed and correctly interpreted only at tumour recurrence, with progression to malignancy in one.

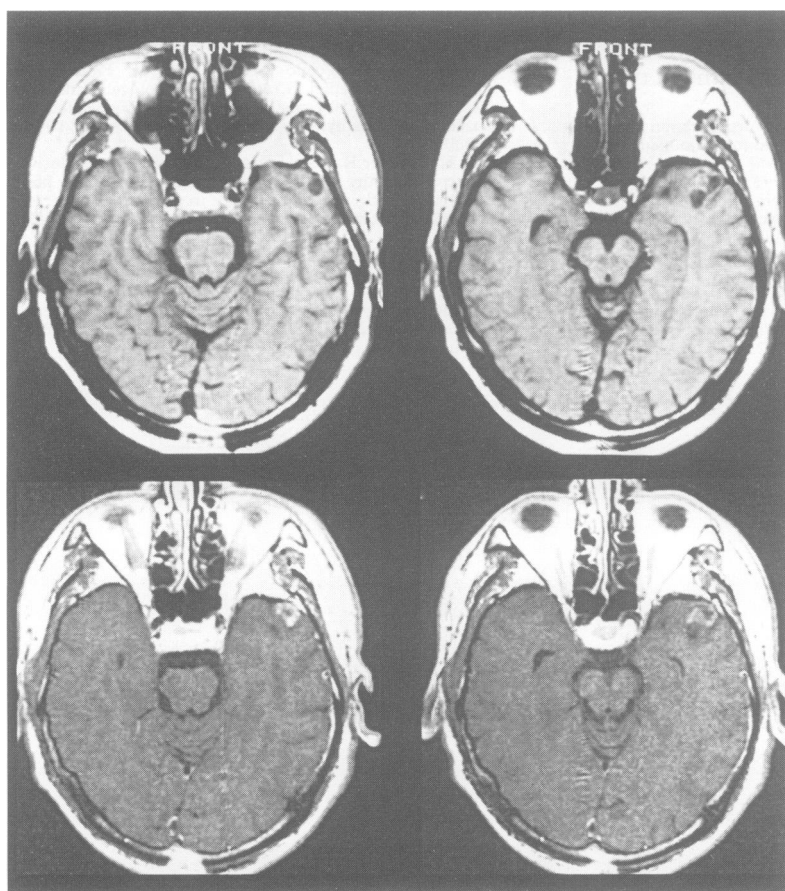


Figure 1 MRI of patient 1 showing a polycystic lesion of about 2 cm in diameter at the surface of the left temporal pole with a ring shaped enhancement. T1 weighted image before (top) and after (bottom) gadolinium contrast.

Patient 1

A 44 year old man presented with a 32 year history of epilepsy and no other clinical manifestation. Seizures were generalised for the first five years, ceased under medication for seven years, and took a complex partial character thereafter. Magnetic resonance imaging disclosed a left temporopolar and superficial polycystic lesion, measuring 2 cm, with a slightly hyperintense nodule and faint enhancement (fig 1). A tumorous infiltrate of the arachnoid was not obvious. Invasive EEG recording showed a left temporal focus and herein favoured the hippocampus. A two thirds temporal lobe resection with hippocampectomy was performed. Histologically, pleomorphic xanthoastrocytoma with leptomeningeal spread was diagnosed. The resected hippocampus showed focal glial dysplasia. Three months after surgery MRI showed no evidence of residual or recurrent tumour. The patient was well and seizure free under continued antiepileptic medication.

Patient 2

A 15 year old girl presented with a three month history of epilepsy without other clinical signs. T1 weighted MRI disclosed an isointense but enhancing, left temporomesial lesion of 2.5 cm. The adjacent arachnoid also showed enhancement. At surgery, a clear demarcation from the brain tissue was lacking. Histologically, a ganglioglioma was diagnosed. Nine months later MRI showed a recurrence

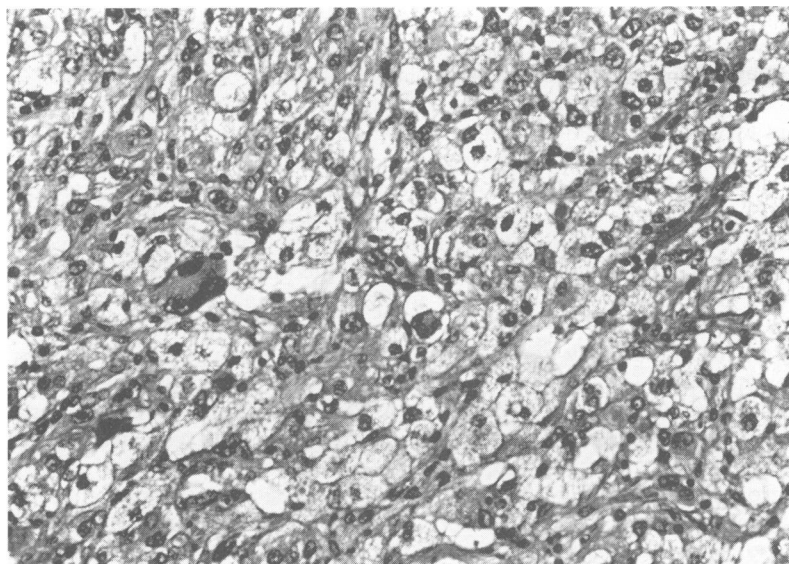


Figure 2 Photomicrograph of pleomorphic xanthoastrocytoma. Note the pronounced pleomorphism of astrocytic cells with large hyperchromatic nuclei and the presence of numerous foamy histiocytes (haematoxylin and eosin $\times 240$).

of 4×2 cm along the medial and inferior resection borders, exhibiting the same signal pattern as initially. The tumour was resected again. The leptomeningeal covering of both the temporomesial region and the adjacent brainstem seemed to be infiltrated but had to be left in place, because of perforating arteries contained in it. The histological diagnosis was that of a malignant pleomorphic xanthoastrocytoma (World Health Organisation (WHO) grade 3). Re-evaluation of the previous specimens also confirmed the diagnosis of pleomorphic xanthoastrocytoma. No adjuvant therapy was performed. Eight months after the second operation MRI showed no evidence of recurrence.

Patient 3

Presenting with seizures, this young woman was first operated on at the age of 15 for a neoplasm initially classified as an atypical menin-

gioma that covered the floor of the left middle cranial fossa and filled out the temporal ventricle horn. Ten years later, although the patient still presented occasional seizures without any other clinical sign, MRI showed tumour recurrence at the posterosuperior and antero-inferior borders of the resection cavity. Two firm tumour nodules were extirpated; there was no infiltration of the arachnoid. Histologically, pleomorphic xanthoastrocytoma was diagnosed. Re-evaluation of the previous specimens confirmed the diagnosis. The postoperative course was uneventful; a clinical follow up is not yet available.

Pleomorphic xanthoastrocytoma was described as a novel clinicopathological entity by Kepes *et al*¹ in 1979. It is a glioma composed of a pleomorphic population of small and large to giant, sometimes multinucleated, cells with abundant cytoplasmatic lipid droplets and a large amount of reticulin fibres, which are partially organised to basal membranes and surround individual cells or groups of cells. According to its usually superficial location with attachment to the leptomeninges and the production of abundant reticulin fibres, pleomorphic xanthoastrocytoma is believed to originate from subpial astrocytes. Despite pronounced pleomorphism—which otherwise suggests malignancy—mitosis and endothelial proliferation are rare, necrosis is absent, and the tumour displays a relatively favourable biological behaviour.¹

A literature survey covering 46 papers yielded 88 different cases of pleomorphic xanthoastrocytoma that fulfill the histological criteria of Kepes *et al*,¹ hence excluding those tumours with a notable amount of necrosis.^{1–11} Pleomorphic xanthoastrocytomas are rare tumours: five were identified by reviewing the slides of 50 patients under the age of 30 years who had had an initial diagnosis of glioblastoma or atypical glioma.² The table summarises the clinical, radiological, and therapeutic data from the medical literature. Imaging usually shows a superficially located, often cystic tumour with a solid, enhancing nodule and little perifocal oedema. Evidence of meningeal infiltration could be a strong diagnostic argument, because meningeal infiltration is much less common in other gliomas, with the exception of the pilocytic astrocytoma.

One of our patients presented with a history of epilepsy that surpasses the longest reported duration of medical history of pleomorphic xanthoastrocytoma by 14 years.³ In patient 3, the diagnosis of an atypical meningioma was put forward in 1981, two years after the first description of pleomorphic xanthoastrocytoma, and revised 10 years later. The tumour in patient 2 was initially interpreted as a ganglioglioma in a typical location, but revised at recurrence only nine months later, now as a malignant pleomorphic xanthoastrocytoma. We explain these misdiagnoses by an insufficient acquaintance with the novel entity and by a sampling failure.

Pleomorphic xanthoastrocytoma has also been confused with neoplasms such as fibrous

Table 1 Pleomorphic xanthoastrocytoma features reviewed from the medical literature

Sex ratio (n = 87):		MRI findings (n = 25):	
Male	53%	Hypo or isointense T1	94%
Female	47%	Hyperintense T1	6%
Age (y)		Gd enhancement	100%
Average	17.5 y	Hyperintense T2	100%
Range	3–66 y	Cystic appearance	52%
Presenting symptoms (n = 80):		Perifocal oedema	36%
Seizures	74%	Intraoperative findings (n = 52):	
Raised ICP	15%	Intimate meningeal contact	60%
Headache	10%	Superficial location	36%
Paraparesis	1%	deep location	4%
Location (n = 88):		Borders well recognisable	71%
Temporal lobe	61%	Borders partially recognisable	13%
Parietal lobe	11%	Borders poorly recognisable	16%
Frontal lobe	9%	Cystic component	77%
Occipital lobe	5%	Firm consistence	80%
Basal ganglia	6%	Follow up (n = 58):	
Combined supratentorial	6%	Average duration	7.5 y
Cerebellum	1%	Surgery only	55%
Thoracic spine	1%	Mean follow up	5.5 y
CT findings (n = 52):		Lethal tumour progression	6%
Hypodense	58%	Surgery + radiotherapy	39%
Isodense	38%	Mean follow up	7.0 y
Hyperdense	4%	Lethal tumour progression	5%
Contrast enhancement	95%	Surgery + radiotherapy	
Cystic appearance	54%	+ chemotherapy	6%
Calcification	11%	Reintervention	38%
Perifocal oedema	31%	Mean interval	7.0 y
		Malignancy at reintervention	15%
		Tumour related deaths	15%

xanthoma (fibrous histiocytoma) of the meninges, giant cell astrocytoma with histiocytic infiltration, and lipidised giant cell glioblastoma multiforme.^{1,2,4} Until recently, the hypothesis has been put forward that pleomorphic xanthoastrocytoma may represent a mesodermal, rather than an astrocytic, neoplasm.⁵ However, there is overwhelming evidence for its astrocytic nature. The tumour invariably exhibits immunoreactivity for glial fibrillary acid protein and can evolve towards a malignant glioma.^{1,2,5,6} These findings led to the inclusion of pleomorphic xanthoastrocytoma as a clinicopathological entity in the recently revised WHO classification of brain tumours.¹² One remarkable case is a patient with temporal pleomorphic xanthoastrocytoma, in whom a second, frontal pleomorphic xanthoastrocytoma developed with a latency of a few years, showing no signs of malignancy, obviously a multilocal manifestation.⁷ Recently, the first pleomorphic xanthoastrocytoma in a case of neurofibromatosis type 1 has been reported.⁸ Within comparable follow up periods, it is surprising to find a similar number of survivors among patients who initially had an incomplete tumour resection and those who had a complete resection. This is best explained by favourable biological tumour behaviour which extends over a period of time that exceeds the considered follow up and thus determines the outcome even of incompletely resected tumours.⁹ The relatively benign biological behaviour of pleomorphic xanthoastrocytoma is also reflected by DNA-cytofluorometric data.¹⁰ As good clinical relief and long courses are found after subtotal surgery, radical surgery should not be sought for at the price of heavy neurological deficit.

Pleomorphic xanthoastrocytoma-like tumours with necrosis exhibit a clearly less favourable prognosis. This justifies the definition of pleomorphic xanthoastrocytoma as a tumour without any considerable amount of necrosis, mitotic activity, or endothelial proliferation. On the other hand, pleomorphic xanthoastrocytoma may undergo progression to a necrotising malignant glioma. In this regard, pleomorphic xanthoastrocytoma and pleomorphic xanthoastrocytoma-like tumours with necrotic changes could represent a single tumour entity, diagnosed at different biological stages. Pleomorphic xanthoastrocytoma that has become malignant exhibits a variable

loss of lipidisation and pleomorphism, and often presents as a malignant astrocytoma or glioblastoma of the small cell type.^{1,2,6} Inversely, however, not all malignant gliomas that histologically exhibit lipidisation, are derived from pleomorphic xanthoastrocytoma. About 38% of the patients were reoperated on because of recurrence after an average course of seven years. Of these patients, 41% showed a progression of pleomorphic xanthoastrocytoma to malignant glioma. Because pleomorphic xanthoastrocytoma can become malignant even after many years of benign behaviour, long term follow up is necessary. There is no obvious difference in outcome between those patients who were treated by surgery alone and those treated by surgery plus radiotherapy. The value of radiotherapy therefore remains unclear and the inclination is to restrict postoperative radiotherapy to cases of recurrent pleomorphic xanthoastrocytoma that histologically present as a malignant glioma.

- 1 Kepes JJ, Rubinstein LJ, Eng LF. Pleomorphic xanthoastrocytoma: a distinctive meningocerebral glioma of young subjects with relatively favorable prognosis. A study of 12 cases. *Cancer* 1979;44:1839-52.
- 2 Heyerdahl Ström E, Skullerud K. Pleomorphic xanthoastrocytoma: report of 5 cases. *Clin Neuropathol* 1983;2:188-91.
- 3 Palma L, Maleci A, Di Lorenzo N, Lauro GM. Pleomorphic xanthoastrocytoma with 18-year survival. Case report. *J Neurosurg* 1985;63:808-10.
- 4 Whittle IR, Gordon A, Misra BK, Shaw JF, Steers AJW. Pleomorphic xanthoastrocytoma. Report of four cases. *J Neurosurg* 1989;70:463-8.
- 5 Paulus W, Peiffer J. Does the pleomorphic xanthoastrocytoma exist? Problems in the application of immunological techniques to the classification of brain tumors. *Acta Neuropathol* 1988;76:245-52.
- 6 Kepes JJ, Rubinstein LJ, Ansbacher L, Schreiber DJ. Histopathological features of recurrent pleomorphic xanthoastrocytomas: further corroboration of the glial nature of this neoplasm. A study of 3 cases. *Acta Neuropathol* 1989;78:585-93.
- 7 Iwaki T, Fukui M, Kondo A, Matsushima T, Takeshita I. Epithelial properties of pleomorphic xanthoastrocytomas determined in ultrastructural and immunohistochemical studies. *Acta Neuropathol* 1987;74:142-50.
- 8 Özek MM, Sav A, Pamir MN, Özer AF, Özek E, Erzen C. Pleomorphic xanthoastrocytoma associated with Recklinghausen neurofibromatosis. *Childs Nerv Syst* 1993;9:39-42.
- 9 Macaulay RJB, Jay V, Hoffman HJ, Becker LE. Increased mitotic activity as a negative prognostic indicator in pleomorphic xanthoastrocytoma. *J Neurosurg* 1993;79:761-8.
- 10 Hosokawa Y, Tsuchihashi Y, Okabe H, et al. Pleomorphic xanthoastrocytoma. Ultrastructural, immunohistochemical, and DNA cytofluorometric study of a case. *Cancer* 1991;68:853-9.
- 11 Herpers MJHM, Freling G, Beuls EAM. Pleomorphic xanthoastrocytoma in the spinal cord. Case report. *J Neurosurg* 1994;80:564-9.
- 12 Kleihues P, Burger PC, Scheithauer B. Histological typing of tumours of the central nervous system. *World Health Organization International Classification of Tumours*. Berlin: Springer, 1993.